REMARKS

The abstract has been amended to delete the word "novel".

The extraneous period in claim 20 has been eliminated and the "such as" recitations separated into new dependent claims. Claim 19 has been amended to correct the Roman numeral.

With respect to the terminology "Lys(iPr,P^4)", the modification of the side chain by attachment of iPr is, according to IUPAC nomenclature, abbreviated as Lys(iPr). During the synthesis of the LHRH antagonists, the ε-amino group still requires protection (P^4) and since both the P^4 and the isopropyl group are attached to the ε-amino group, it is respectfully submitted that the correct abbreviation is Lys(iPr,P^4).

In view of these changes and traversal, it is respectfully submitted that the rejection under 35 U.S.C. § 112 can now be withdrawn.

The rejection of claim 26 under 35 U.S.C. § 103 over Funk in view of O'Neill is respectfully traversed.

The Office Action has taken the position that Funk differs from the instant claim by showing a compound in which the N-terminus is acetyl rather than Boc. It is asserted that the substitution was obvious based on Boc being a potential protecting group and that one "would have been motivated to make the Boc protected peptide in order to make a compound which would function similarly in the synthesis of LHRH analogs" with a reasonable expectation of success. It is respectfully submitted that the proposed motivation is an after-the fact justification since it presumes that one skilled in the art

would want to make something which would "function similarly" without any suggestion or proposal as to why the skilled person would have that desire. Funk teaches that compounds used an intermediate for the preparation of compound III are always esterified at the C-terminus. In compound III, the N-terminus is Q which is defined to be either Ac or THF-Gly. If one skilled in the art wanted to make a compound where Q is Ac, then it is not apparent why a Boc protected intermediate rather than an Ac intermediate would be employed (even if one ignores the ester at the other terminus). Why one skilled in the art would ever be motivated to employ a Boc protected group when it is desired that Q be THF-Gly is also not apparent. The THF-Gly analogue is made from its methyl ester as shown in Examples 26-28 or from the Boc methyl ester in Example 25. All of the N-terminus protected compounds III and there is no reason to make the N-protected C-nonprotected tripeptide of claim 26. There is clearly no justification or motivation for making the tripeptide of the instant claim 26. Whatever justifications may be intoned after reading the present application cannot substitute for a prospective justification as of the filing date of this application without using the application as a template.

Further, the conversion yield in Funk of the ester to the non-ester when Q is THF-Gly is 50% and a similar yield would be expected when Q was Ac. In the invention, the compound of claim 26 permits the same Ac product to be obtained in a yield of 70%. This is surprising and unexpected. Nothing in the prior art teaches or suggests that the tripeptide of the instant claim 26 could contribute to this unexpected superiority.

In light of all of the foregoing, it is respectfully submitted that claim 26 is allowable.

The rejection of claims 14-16, 18, 20-22, 25 (now canceled) and 26 under 35 U.S.C. § 103(a) over Funk in view of O'Neill, Hubbs and Veber is respectfully traversed.

In the first instance, it is not understood how the additional references Hubbs and Veber are applicable to the claim 26 rejection. The cited teachings of both Hubbs and Veber add nothing to the rejection of this claim over Funk in view of O'Neill which has been discussed above and shown to be insufficient.

The remaining claims in this rejection are process claims, all of which are dependent, directly or indirectly, on claim 14. Claim 14 recites a three-step process for making the compound of claim 26 which is then optionally converted into the compound of now canceled claim 25. The cited references do not teach or suggest the three-step process of claim 14.

The Office Action acknowledges that the claimed process differs from that of Funk in that Funk does not, *inter alia,* teach the use of HONSu in the coupling step. To overcome this deficiency, the Office Action relies on Hubbs. The passage in Hubbs quoted in the Office Action can be simplified as stating that "the condensation reaction of the two fragments can be accomplished [by] treatment of the two peptide fragments with ...an activating agent [such as HONSu]." The applicability of this teaching is not appreciated. While it may be pertinent if what was being claimed is the condensation of two peptide fragments in the presence of HONSu, claim 14 step (a) constitutes reacting Boc-D-4ClPhe-OH with HONSu. It is respectfully submitted that the proposed motivation in the Office Action that one skilled in the art would have used HONSu in the coupling of two fragments to inhibit racemization of the product does not appear to have any relevance to the process actually claimed herein.

It is noted that the Office Action makes no attempt to point out where Funk teaches the sequence of the three mandatory steps in claim 14, other than making some vague reference to "basic methods claimed". But there is no teaching or suggestion in Funk, whether considered alone or combination with the other references, which teaches or suggests the specific consecutive steps recited in claim 14.

The following table compares the instant process and that of Funk where Q is THF-Gly starting from the same material:

Acetate by the method of the invention starting from Boc-D-4ClPhe-OH	Yield, %	2-R,S-THF-Gly analogue by to the method of US 5,710,246 starting from Boc-D-4ClPhe-OH	Yield, %
Boc-D-4ClPhe-OSu	85	Boc-D-4ClPhe-D-3-Pal-O-Me	80
Boc-D-4ClPhe-D-3Pal-OH	80	Boc-D-2Nal-D-4ClPhe-D-3Pal-OMe	80
Boc-D-2Nal-D-4ClPhe-D-3Pal-OH	90	2R,S-THF-Gly-D-2Nal-D-4ClPhe-D-3Pal-O-Me	40
Ac-D-2Nal-D-4ClPhe-D-3Pal-OH	70*	2R,S-THF-Gly-D-2Nal-D-4ClPhe-D-3Pal-OH	50
Total yield:	47.6%	Total yield:	12.8%

*In respect of Boc-D-4ClPhe-D-3Pal-OH

There is no reason to assume that the yield would significantly vary when Q is Ac (making the final product the same in both columns). One skilled in the art would not have expected the superiority of the claimed method.

Claims 14-26 have been rejected under 35 U.S.C. § 103(a) over Funk in view of O'Neill, Hubbs and Veber and in further view of Gefter. This rejection is also respectfully traversed. Gefter does not cure any of the deficiencies of the four reference combination and therefore cannot serve to render any of these claims obvious. In that connection, it is noted that Gefter has been cited only to show that AA2 can be a natural amino acid but any reference to AA2 first appears in instant claim 15, not claim 14.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: June 28, 2007

Respectfully submitted,

By /Edward A. Meilman/
Edward A. Meilman
Registration No.: 24,735
DICKSTEIN SHAPIRO LLP
1177 Avenue of the Americas
New York, New York 10036-2714
(212) 277-6500
Attorney for Applicant